GEORGIA INSTITUTE OF TECHNOLOGY
OFFICE OF CONTRACT ADMINISTRATION
SPONSORED PROJECT INITIATION

Date: 2/24/81

Project Title: The Chemistry of New Functional Groups In Enzymes

Project No: G-33-N03

Project Director: Dr. Edward M. Burgess

Sponsor: DHEW/PHS/NIH - National Institute of General Medical Sciences; Bethesda, Maryland 20014

Agreement Period: From March 1, 1981 Until February 28, 1982 (11 year)

Type Agreement: Grant No. 5-R01-GM12672-11

Amount: $ 89,421 New PHS Funds (G-33-N03)
11,967 GIT Contribution (G-33-357)

$101,388 TOTAL

Reports Required: Annual Progress Reports with Continuation Applications; Terminal Progress Report upon Grant Expiration

Sponsor Contact Person (s):

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Contractual Matters
(thru OCA)

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Grants Management Specialist
Office of Associate Director for Program Activities
National Institute of General Medical Sciences
Bethesda, Maryland 20014

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NOTE: Continuation of G33-N02 (year 10)

Defense Priority Rating: None

Assigned to: Chemistry (School/Laboratory)

COPIES TO:

Project Director
Division Chief (EES)
School/Laboratory Director
Dean/Director-EES
Accounting Office
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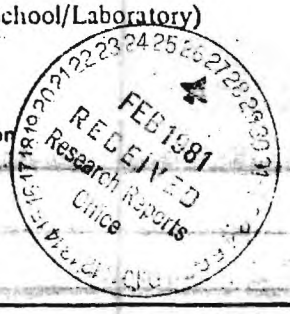
Library, Technical Reports Section
EES Information Office
EES Reports & Procedures
✓ Project File (OCA)
Project Code (GTRI)
Other C. E. Smith



GEORGIA INSTITUTE OF TECHNOLOGY OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION SHEET

Date 7/11/83

Project Title: The Chemistry of New Functional Groups in Enzymes

Project No: G-33-N03

Project Director: Dr. Edward M. Burgess

Sponsor: DHEW/PHS/NIH - National Institute of General Medical Sciences
Bethesda, MD 20014

Effective Termination Date: 2/28/82 (11 year)

Clearance of Accounting Charges: 2/28/82

Grant/Contract Closeout Actions Remaining:

NONE

- [ ] **Final Invoice and Closing Documents**
- [ ] **Final Fiscal Report**
- [ ] Final Report of Inventions
- [ ] Govt. Property Inventory & Related Certificate
- [ ] Classified Material Certificate
- [ ] Other _____

NOTE: Follow-on Project (12 year) - G-33-N04

Assigned to: Chemistry (School/~~Laboratory~~)

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RAN
~~Administrative Coordinator~~
Research Property Management
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Computer Input
Project File
Other GTRI

FORM OCA 10-78A

APPLICANT: REPEAT GR. NUMBER SHOWN ON PAGE 1	GR. NUMBER	
SECTION IV—SUMMARY PROGRESS REPORT	5 R01 GM12672-12	
PRINCIPAL INVESTIGATOR OR PROGRAM DIRECTOR (Last, First, Initial)	PERIOD COVERED BY THIS REPORT	
Burgess, Edward M.	FROM	THROUGH
NAME OF ORGANIZATION	3/1/82	2/28/83
Georgia Institute of Technology		

TITLE (Repeat title shown in item 1 on first page)

The Chemistry of New Functional Groups in Enzymes

1. List all publications, not previously reported, resulting from work supported by this grant (author(s), title, page numbers, year, journal or book). List manuscripts separately as submitted for publication or accepted for publication.
2. Provide two reprints of publications not previously submitted to the awarding unit.
3. Progress Report. (See instructions)

Final Report
G-33-N03/Burgess

1. None

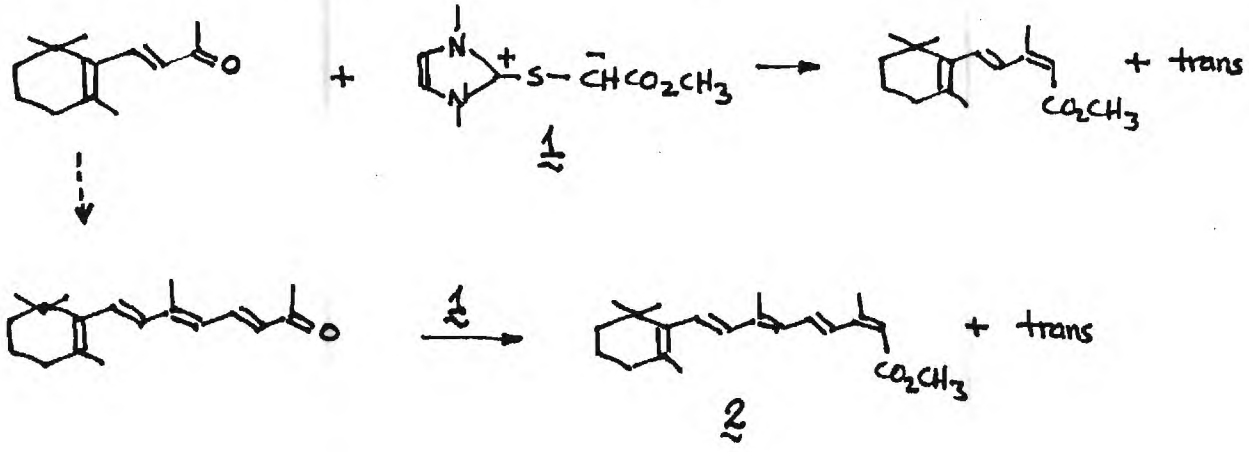
2. Not Applicable

3. Progress Report:

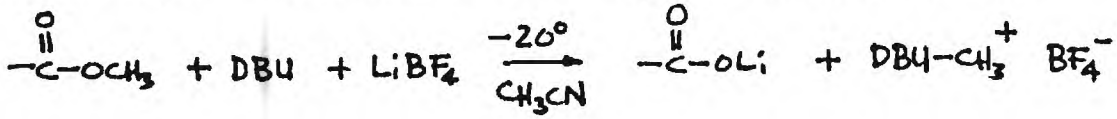
1. The scientific goals are as originally stated.

2. Thione Methylides

We have optimized the conditions for reaction of the ylide, 1, (generated in situ) with ketones. In model studies, using DBU as the base and acetonitrile solvent the stereochemistry of the quasi-Wittig is predominately cis (cis/trans, 3:1)



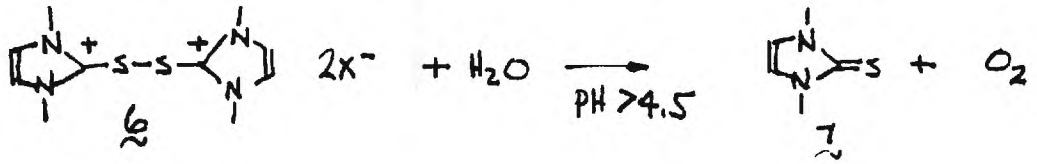
Extension of this reaction to 13-cis retenoic ester, 2, gave the stereoisomeric products in a cis/trans ratio of 2:1. $LiBI_4$ was added in an attempt to increase the amount of cis-product as had been previously observed in the reaction of 1 with aldehydes. Since the reaction of 1 with ketones is much slower than with aldehydes the added salt resulted in demethylation. This reaction turns out to be very facile and we plan to investigate its scope. It would seem to be for superior to the Eschenmoser



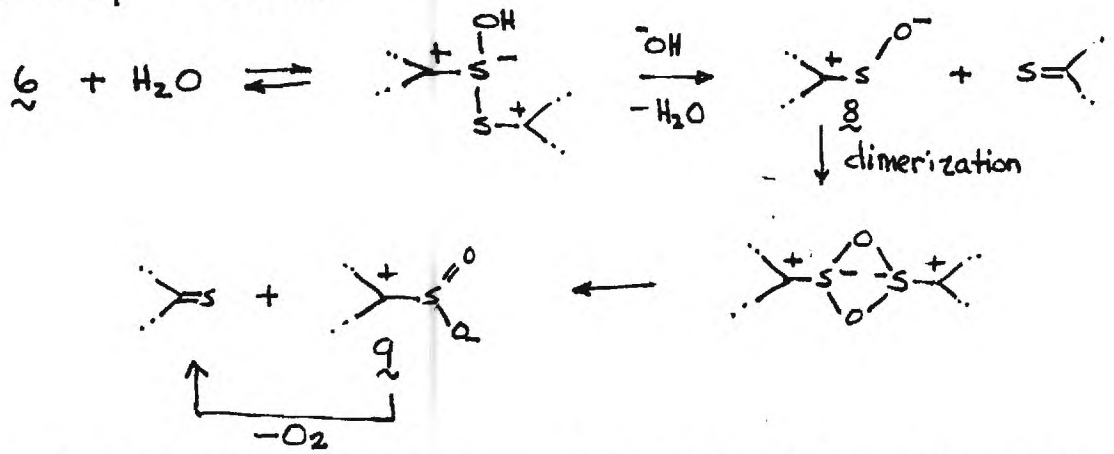
collidine-LiI procedure.

Electrophilic Reactions of Dimethylimidazolethione Disulfide Dications.

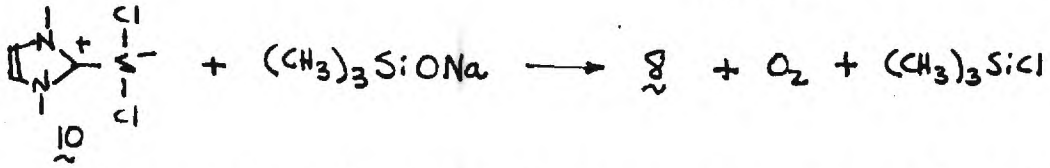
We have continued out investigation of the usual reaction:



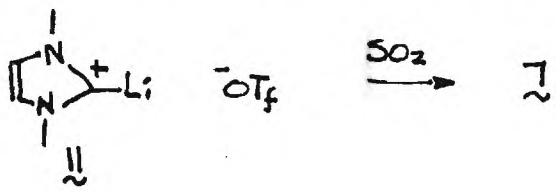
which stands unique among organic reactions which give dioxygen and serves as an interesting model for the proposed sulfenic acid intermediates in certain enzymatic reactions. As a working hypothesis we envisioned this redox reaction to occur via the following mechanism:



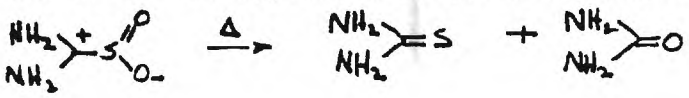
and then attempted the synthesis of 8 and 9 by other methods. The reaction of the sulfurane, 10, with sodium trimethylsilanoate in CH_2Cl_2 at -78° led to the rapid evolution of dioxygen and formation of trimethylsilyl chloride, and 7. If 8 was formed it



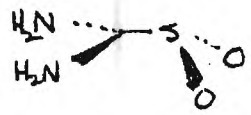
underwent disproportionation at this low temperature. Next, dimethylimidazolium triflate was treated with BuLi in THF at -60° to give the eithio-cation, 11, which upon exposure to sulfur dioxide again gave 7 which suggests that the conversion of 9 to dioxygen is extremely facile. In fact, the commerically available "thiourea



dioxide", 12, upon reflux in dry acetonitrile for 12 hrs gave a 3:1 mixture of thioura and uera. It appears that sulfenes substituted with electron donor groups



are capable of facile chelatropic explusion of dioxygen - but in what spin state? A MINDO-3 SCG calculation with total energy-geometry optimization indicated that a non-planar singlet (pyranidal at sulfur) structure for 12 which agrees with the known x-ray crystallography for 12. With an energetic expenditure of ca. 18 kcals



this non-planar structure can be converted to a planar dioxide and this change in geometry leds to a HOMO-LUMO crossing and the passage of 12 into a triplet manifold! Dioxygen is then expelled as a ground state triplet in an exothermic step.

This class of reaction is not limited to 6. Oxidation of tris(dimethylamino) phosphine sulfide, 13, with $NOBF_4$ gives a disulfide which also oxidizes water.

$$\underset{\underset{13}{\sim}}{[(CH_3)_2N]_3\overset{+}{P}-S-S-\overset{+}{P}[(CH_3)_2N]_3}\ 2X^- \xrightarrow[-HX]{H_2O} [(CH_3)_2N]_3\overset{+}{P}-S^- + O_2$$

We continue to investigate the oxidative behavior of 6 and 13.

3. During the forthcoming year we wish to explore

   a. the scope of the oxidative ability of the electrophilic disulfides derived from dimethylimidazolethione and phosphine sulfides

   b. other reactions of thione methylides with functional groups other than carbonyl.

   c. furhter details of the chemical oxidation of water to oxygen.

The undersigned agrees to accept responsibility for the scientific and technical conduct of the project and for provision of required progress reports if a grant is awarded as a result of this application.

12-28-81
date

Edward M. Burgess
Principal Investigator